KOUZARIDES
Appl. No. 09/700,417
September 15, 2003

REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The claims have been revised to define the invention with additional clarity. That the claims have been amended should not be construed as an indication that Applicant agrees with any view expressed by the Examiner. Rather, the revisions have been made to advance prosecution and Applicant reserves the right to pursue any deleted subject matter in a continuation application.

35 USC 112, 2nd paragraph

Claims 1-10 stand rejected as allegedly being indefinite in view of the use of the terms "P/CAF" and "E2F". Withdrawal of the rejection is submitted to be in order for the reasons that follow.

MPEP 2173.02 states;

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

In the light of the specification, the prior art and the understanding of the skilled person, the terms P/CAF and E2F have a clear and definite meaning.

The Examiner alleges that other laboratories may name the same proteins using different names. This is not the case. P/CAF and E2F are the standard terms that are used in the art to designate these proteins. Although nomenclature may be ambiguous when proteins are first identified, for example, because, in the absence of a standard nomenclature, different laboratories may use different names for the same protein, any discrepancies are swiftly resolved and the field adopts a standard name for a new protein. Once this standard name has been agreed, it is used unambiguously and ubiquitously in the art to refer to a particular protein. Other names are not then used.

E2F and P/CAF were well known at the time of the invention and the present invention does not relate to the discovery or isolation of these proteins. Unlike the situation when proteins are identified for the first time, the terms E2F and P/CAF were standard terms at the time of the invention and had a clear and generally accepted meaning in the art.

The Examiner alleges that it is not clear if P/CAF and GCN5 are synonyms or represent different proteins.

The specification states;

> *There are now four families of enzymes with such activity. These are GCN5 and P/CAF (Brownell, et al (1996), Cell, 84: 843-831 and Yang, et al (1996), Nature, 382: 319-324), CBP and p300 (Bannister and Kouzarides (1996), Nature, 384: 641-643 and Ogryzko, et al (1996), Cell, 87: 953-959), SRC1 and ACTR (Chen, et al (1997), Cell, 90: 569-580 and Spencer, et al (1997), Nature, 389: 194-198) and TAF250 (Mizzen, et al (1996), Cell, 87: 1261-1270).*

It is clear from this passage that GCN5 and P/CAF are different proteins (note 'GCN5 and P/CAF' and not 'GCN5 or P/CAF') which are members of one of the four families of histone acetylases.

Furthermore, since both GCN5 and P/CAF are known in the art, the skilled person would be fully aware that they are distinct proteins, as confirmed by the references cited in the specification.

The Examiner further alleges that it is unclear if the recitation of P/CAF and E2F refers to two specific proteins or to two families of proteins. As described above, the meaning of these terms is well known to the skilled person, who would clearly understand the scope of the present claims.

Reconsideration of the rejection is therefore requested.

35 USC 112, 1st paragraph

Claims 1-10 stand rejected as allegedly lacking written description in view of the use of the terms "P/CAF" and "E2F". The rejection is traversed.

The present invention concerns the acetylation of E2F by P/CAF. The specification indicates that acetylation by P/CAF modulates the activity of E2F and the inhibition of acetylation may be useful in the inhibiting cell proliferation.

It should be noted that the specification does not disclose either P/CAF or E2F for the first time: both P/CAF and E2F were well-known in the art prior to the invention. The claimed assay methods, which relate to the interaction of these proteins, are, however, novel and unobvious over the prior art.

Although the claims are directed to assay methods, they refer to a genus of P/CAF polypeptides which have the human P/CAF protein sequence and a genus of E2F polypeptides which have one of the human E2F1, E2F2, E2F3, E2F4 or E2F5 protein sequences.

It is noted that the interim guidelines for Written Description on the USPTO website state:

> *The absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. 112, para. 1, for lack of adequate written description.*

As discussed above, the terms P/CAF and E2F are well established in the art and have a definite meaning to the skilled person. The Examiner suggests that the specification fails to define 'wild-type' P/CAF and E2F in terms of amino acid sequence. However, the terms P/CAF and E2F, as they are understood in the art, define amino acid sequences and further definition is unnecessary. Human P/CAF is explicitly disclosed in the specification, along with mutant versions of the protein which have an inactivated acetyltransferase domain. Human E2F1, E2F2, E2F3, E2F4 and E2F5 are explicitly disclosed and discussed on page 7, line 10, to page 9, line 10. These species are fully representative of their respective genuses.

In particular, the Examiner suggests that the recitation of P/CAF encompasses a genus of histone acetylase proteins of unspecified structure. However, human P/CAF is a particular histone acetylase protein with a defined sequence which was well known in the art long before the filing of the present application (see, for example, Yang, et al (1996),

Nature, **382**: 319-324). The term P/CAF would be understood by a skilled person to refer to a specific polypeptide and not to encompass any histone acetylase.

> The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999)

The Examiner alleges that no common structural attributes identify members of the genus. However, P/CAF polypeptides have the sequence of human P/CAF and E2F polypeptides have one of the sequences of human E2F1 to E2F5. All these sequences are known in the art.

There is actual reduction to practice of human P/CAF. The human P/CAF sequence is a common structural feature which identifies all members of the genus. The genus is therefore both narrow and clearly defined and encompasses a narrow range of species with similar attributes and human P/CAF is representative of this genus.

There is actual reduction to practice of human E2F1. All the five species of E2F polypeptide which are encompassed by the genus possess the characteristic domains of members the E2F family, including DNA binding, dimerisation, 'marked box' and transcriptional activation domains (see page 7, lines 10-23, of the specification). These are common structural features which identify all members of the genus of 'E2F polypeptides'. This genus is therefore both narrow and clearly defined and encompasses a narrow range of species which are closely related and have similar attributes. Human E2F1 is representative of this genus.

Each of the P/CAF and E2F genuses is stated by the Examiner to be highly variant because an unlimited amount of structural alterations are tolerated for the individual members of the genus. However, as described above, the terms P/CAF and E2F, as used in the present claims, would not be understood by those skilled in the art as encompassing any protein, but rather would be understood to refer to specific proteins. The genuses encompassed by these terms are therefore not highly variant and tolerate little, if any, structural alteration, as alleged by the Examiner.

Weighing all factors, 1) closely related structures of the proteins which fall within the P/CAF and E2F polypeptides, respectively 2) the narrow breadth of these genuses and 3) the level of knowledge and skill in the art at the time of the invention, one of skill in the art would reasonably conclude that the genuses of P/CAF and E2F polypeptides are clearly defined and that Applicant was in possession of claimed methods employing these genuses.

Claim 10 is rejected as lacking written description because the term 'component' is highly variant.

As stated above, the present invention relates to the acetylation of E2F by P/CAF and in particular to the identification of agents which disrupt this interaction. A particular 'additional component' in a formulated composition is not essential to the claimed invention.

Claim 10 itself is drawn to a genus, i.e., any of a variety of methods for identifying a modulator of the interaction of P/CAF and E2F and then formulating this modulator into a composition which has at least one other constituent.

There is no substantial variation within the genus encompassed by this claim because there are a limited number of ways to practice the process steps of the claimed invention. All the steps of the process of claim 1 are required along with an additional process step. Whether or not the term 'additional component' is broad and variant is irrelevant, in light of the invention. The identity of the additional component of the composition is not essential and a skilled person is readily able to produce compositions comprising the agent along with other 'additional components'. The conclusion of one of skill in the art would therefore be that Applicant was in possession of the claimed method.

Reconsideration of the rejection is therefore requested

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

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Respectfully submitted,

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